

AMENDMENT

Pursuant to the accompanying filing under 37 C.F.R. §1.137(b), applicants respectfully request entry of the amendments previously refused by the examiner.

REMARKS

I. Status of the Claims

Claims 23-42 are pending in the application and stand rejected, variously, under 35 U.S.C. §112, first and second paragraphs. The specific grounds of rejection, and applicants' response thereto, are set out in detail below.

II. Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 23 and 25-42 were rejected under the second paragraph of §112 as allegedly indefinite. It is believed that the only remaining rejection, following applicant's previous submission, is that of claim 24. Claim 24 is rejected for the term "stringent hybridization."¹ Applicants traverse. The term stringent hybridization is well known to those of skill in the art and, as of 1997, hardly needed any particular explanation to those working in this field. However, applicants direct the examiner to page 29 of the specification that reduced stringency includes 55°C. Thus, high stringency would be higher than this figure. The examiner also argues that one must also need to know wash conditions to know stringency. While true, one of skill in the art can select not only temperature, but ionic strength and wash conditions, and still achieve "high stringency."

¹ Claim 24 has been canceled. However, as the term is now part of claim 23, the rejection is addressed to the extent that it would apply to amended claim 23.

Reconsideration and withdrawal of each of the preceding rejections is respectfully requested.

IV. Rejections Under 35 U.S.C. §112, First Paragraph

A. Written Description

Claims 23-42 stand rejected under the first paragraph of §112 as allegedly encompassing subject matter not within the possession of applicants at the time of filing. Applicants traverse.

The examiner main point appears to be that the claims encompass nucleic acids “that are not structurally related to SEQ ID NO:1.” While that statement is traversed with respect to the claims previously submitted, applicants submit that it is moot in light of the amendments offered here, namely that the claimed derivatives hybridize to SEQ ID NO:1 under highly stringent conditions. Thus, it is not the case that “any deletion, substitution or addition” is encompassed. The rejection also is based, at least in part, on the alleged failure of applicants to define the hybridization conditions. As discussed above, claim 23 now recites “highly stringent” conditions, and this term *is*, in fact, defined by the specification as higher than 50°C.

Finally, the examiner argues that no “deletions, insertions, or point mutations [are] described in the specification ... encoded a protein that retained the activity of SEQ ID NO:2.” This fact, even if assumed true, does not mean that applicants did not possess the subject matter of the rejected claims. It simply means that a working example was not provided; however, it is black letter law that examples are, in fact, *not* required. *In re Borkowski*, 164 USPQ 642 (CCPA 1970). One of skill in the art would not doubt, given the present disclosure, that derivatives satisfying the limitations of the claims, could be created.

Having addressed each of the examiner’s stated concerns, applicants respectfully request reconsideration and withdrawal of the rejection.

B. Enablement

Claims 23-42 are rejected under the first paragraph of §112 as allegedly lacking enablement. The examiner argues that since (a) the phenotype of Ls-transgenic plants is unknown, and that (b) only loss of function derivatives have been created, it would take undue experimentation to use the claimed invention. Applicants traverse.

Regarding the examiner first point, applicants submit that the present application clearly demonstrates that inhibiting expression of the Ls gene product reduces shoot formation, petal formation, and abscission zone formation. Thus, the inventors have made a significant contribution regarding the identification of the Ls gene's role in these activities. One of ordinary skill in the art would accept, on its face, that this gene clearly plays an important role in shoot formation, petal formation, and abscission zone formation. As such, it would be acknowledged that increasing expression of the Ls gene would lead to increased shoot formation, petal formation, and abscission zone formation. Hence, though not proven, the phenotype of the plant can in fact be predicted to at least some degree.² In sum, the examiner has not offered any evidence to support the conclusion that one of skill in the art could not predict the phenotype of transgenic plants expressing Ls genes or antisense constructs, and thus, the invocation of *Genentech v. Novo Nordisk* is improper.

The other issue raised by the examiner – lack of derivatives that retain function – presents a similar situation with regard to enablement. Applicants acknowledge that the specification does not demonstrate derivatives that retain function. However, this is a far cry from establishing non-enablement. One of skill in the art is more than capable of making small deletions, insertions, truncations, fusions, *etc.*, each of which retain the ability to promote shoot

² Applicants contest the examiner's assertion that applicants have admitted that the phenotype of these transgenic plants is unpredictable.

formation, petal formation, and abscission zone formation. Again, the examiner has not offered any *evidence* as to why one of skill in the art would *not* be able to achieve make derivatives as claimed. As such, the examiner has not met the PTO's burden, required before the applicant is tasked with producing additional evidence in support of enablement. *In re Marzocchi*, 169 USPQ 370 (CCPA 1971).

Having addressed each of the examiner's stated concerns, applicants respectfully request reconsideration and withdrawal of the rejection.

C. Declaration

Applicants now provide the declaration of Dr. Nikolaus Theres, the inventor. As discussed in the declaration, one of skill in the art could make various modifications to the polypeptide encoded by SEQ ID NO:2, known as the *Lateral suppressor* gene product, while retaining the function of that molecule, *i.e.*, increased shoot formation, petal formation, and abscission zone formation. A number of experiments are described in support of this position.

First, a tag was inserted in the NH terminus of the Ls gene product. This modification resulted in the insertion of a total of 33 basepairs, encoding the amino acids SYPYDVPDYAR. This construct was introduced via *Agrobacterium*-mediated transformation into the tomato lateral suppressor (*ls¹/ls¹*) mutant. Fourteen transgenic tomato lines containing at least one copy of the construct were analyzed for side-shoot and petal development. Of the 14 transgenic lines, four developed side-shoots in every leaf axil of the primary shoot, and a complete whorl of petals on the flowers. Five additional lines developed side-shoots in more than 60% of the leaf axils of the primary shoot, and a nearly complete whorl of petals on the flowers. The remaining 5 lines

showed a low degree of side-shoot and petal development. This result demonstrates that the modified gene has retained the biological activity of the *Lateral suppressor* gene.

Another experiment looked at the ability of a homologous *Lateral suppressor* gene product from *Arabidopsis* to complement a defect in a tomato *Lateral suppressor* gene product. Sequence analysis revealed that the *Arabidopsis Lateral suppressor* gene (*LAS*) encodes a protein with 50.5% identity to the orthologous gene from tomato (*Ls*). A test for functional complementation between these two distantly related plant species was performed. Four independent transgenic lines harbouring at least one complete copy of the *LAS* gene were established. Two transgenic lines developed side-shoots in almost every leaf axil and a whorl of petals as well as abscission zones on all flowers. The two additional lines developed side-shoots in only a fraction of their leaf axils, and also showed an incomplete restoration of the wild-type flower phenotype. Inheritance of the complementation phenotype was analyzed in one transgenic line harbouring a single copy T-DNA insertion. Among 19 plants of the self-pollinated progeny, 14 plants showed complementation, and 5 plants had the *Lateral suppressor* phenotype. By Southern analysis, the T-DNA was detected only in those plants showing complementation. This result is consistent with the assumption that a single-copy T-DNA insertion, segregating in a Mendelian fashion, rescues the *Lateral suppressor* phenotype.

Dr. Theres also describes an experiment using the powerful cauliflower mosaic virus enhancer element to drive expression of the *Lateral suppressor* gene product using the endogenous *Lateral suppressor* promoter. A transgenic plant developed side-shoots in some of their leaf axils and an incomplete whorl of petals on its flowers, indicating a partial complementation. Furthermore, many additional shoots developed from the upper surface of the

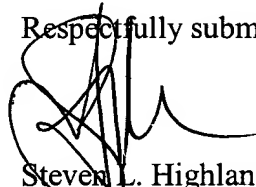
leaves and the leaf petioles. The result of this experiment suggests that overexpression of the *Lateral suppressor* gene leads to the formation of ectopic shoots during leaf development.

Together, these experiments further argue in favor of the skilled artisan and their ability to both recognize and achieve the full scope of applicant's claimed invention.

V. Conclusion

In light of the foregoing, applicants respectfully submit that all claims are in condition for allowance, and an early indication to that effect is earnestly solicited. Should Examiner Mehta have any questions regarding this submission, a telephone call the undersigned is invited.

Respectfully submitted,



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APPENDIX A: Marked Up Copy of Claims (From Prior Submission)

23. (Amended) An isolated nucleic acid molecule comprising:
- (a) a nucleic acid having the nucleotide sequence of SEQ ID NO:1 or a nucleic acid complementary to said nucleotide sequence, wherein the nucleotide sequence encodes a polypeptide having the biological activity of controlling side-shoot formation, petal formation, and abscission zone formation;
 - (b) a fragment or derivative of said nucleic acid or said complementary nucleic acid, wherein the fragment or derivative encodes a polypeptide having the biological activity of controlling side shoot formation, petal formation, and abscission zone formation[; or
 - (c) a nucleic acid that hybridizes], said fragment or derivative hybridizing with said nucleic acid or said complementary nucleic acid[, wherein said hybridizing nucleic acid, or nucleic acid complementary to said hybridizing nucleic acid, encodes a polypeptide having the biological activity of side-shoot formation, petal formation and abscission zone formation] under highly stringent conditions.
24. (Canceled) The nucleic acid molecule of claim 23, wherein said hybridizing nucleic acid hybridizes with the nucleotide sequence of SEQ ID NO:1 under high stringency conditions.
32. (Amended) A method for generating a plant having [modified] increased or suppressed side-shoot formation, petal formation and abscission zone formation, the method comprising:
- integrating a nucleic acid molecule of claim 23 into the genome of a plant cell or a plant tissue for [modifying] increasing or suppressing side-shoot formation, petal formation and abscission zone formation; and
- regenerating the resulting plant cell or plant tissue into a regenerated plant, wherein the regenerated plant expresses [modified] increased or suppressed side-shoot formation, petal formation and abscission zone formation.

35. (Amended) The method of claim 32, wherein the integrating step [further] comprises integrating the nucleic acid molecule in an antisense orientation relative to an endogenous sequence[that modifies side-shoot formation, petal formation, and abscission zone formation].
36. (Amended) The method of claim 32, wherein the integrating step [further] comprises integrating the nucleic acid molecule in a sense orientation relative to an endogenous sequence[that modifies side-shoot formation, petal formation, and abscission zone formation].
37. (Amended) The method of claim 32, wherein the integrating step [further] comprises integrating the nucleic acid molecule into a genomic region of a homologous endogenous gene by homologous recombination.

APPENDIX B: Clean Copy of Pending Claims (Unofficial)

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23. An isolated nucleic acid molecule comprising:
- (a) a nucleic acid having the nucleotide sequence of SEQ ID NO:1 or a nucleic acid complementary to said nucleotide sequence, wherein the nucleotide sequence encodes a polypeptide having the biological activity of side-shoot formation, petal formation, and abscission zone formation;
 - (b) a fragment or derivative of said nucleic acid or said complementary nucleic acid, wherein the fragment or derivative encodes a polypeptide having the biological activity of side shoot formation, petal formation, and abscission zone formation, said fragment or derivative hybridizing with said nucleic acid or said complementary nucleic acid under highly stringent conditions.
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25. The nucleic acid molecule of claim 23, wherein said polypeptide has the amino acid sequence of SEQ ID NO:2.
26. The nucleic acid molecule of claim 23, wherein the nucleic acid has the nucleotide sequence of SEQ ID NO:1.
27. A vector comprising a nucleic acid molecule of claim 23.
28. A transformed plant cell comprising a nucleic acid molecule of claim 23, wherein the nucleic acid molecule is integrated in the genome of the plant cell.
29. A transformed plant cell according to claim 28, which can be regenerated into a seed producing plant.
30. A transformed plant tissue comprising the transformed plant cell according to claim 28.

31. A transformed plant tissue according to claim 30, which can be regenerated it to a seed producing plant.

32. A method for generating a plant having increased or suppressed side-shoot formation, petal formation and abscission zone formation, the method comprising:

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integrating a nucleic acid molecule of claim 23 into the genome of a plant cell or a plant tissue for increasing or suppressing side-shoot formation, petal formation and abscission zone formation; and
regenerating the resulting plant cell or plant tissue into a regenerated plant, wherein the regenerated plant expresses increased or suppressed side-shoot formation, petal formation and abscission zone formation.

33. The method of claim 32, wherein the regenerated plant expresses suppressed side-shoot formation, petal formation, and abscission zone formation.

34. The method of claim 32, wherein the regenerated plant expresses increased side-shoot formation, petal formation, and abscission zone formation.

35. The method of claim 32, wherein the integrating step comprises integrating the nucleic acid molecule in an antisense orientation relative to an endogenous sequence.

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36. The method of claim 32, wherein the integrating step comprises integrating the nucleic acid molecule in a sense orientation relative to an endogenous sequence.

37. The method of claim 32, wherein the integrating step comprises integrating the nucleic acid molecule into a genomic region of a homologous endogenous gene by homologous recombination.

38. The method of claim 32, wherein the regenerated plant is a tomato plant, a rape plant, a potato plant, or a snapdragon plant.
39. A plant obtained by the method according to claim 32.
40. A seed obtained from a plant according to claim 39.
41. A plant comprising a transformed plant cell according to claim 28.
42. A seed obtained from the plant according to claim 41.